

## CLAIMS

What is claimed is:

1. An automated flinch-detection apparatus for measuring spatial displacement  
5 of an animal's paw injected with irritant, comprising:
  - an electromagnetic detecting assembly having
    - a transmitting oscillator for generating electrical current;
    - an electromagnetic transmitter coil coupled to the oscillator for generating an electromagnetic field;
  - 10 an electromagnetic receiving coil placed in a linear plane directly below the transmitter coil;
    - a first, receiving amplifier connected to the receiving coil;
    - an amplitude detector connected to the receiving amplifier;
    - 15 a second amplifier connected to the amplitude detector;
  - 15 a metal object attached to the animal's paw; and
    - a cylindrical observation chamber of a diameter not greater than the diameter of the generated magnetic field, said chamber placed directly over the receiving/transmitting coil assembly,  
wherein the current generated by the transmitting oscillator circulates in the  
20 transmitter coil, creating an electromagnetic field that penetrates the metal object, creating eddy currents perturbing the electromagnetic field, said fluctuating perturbations being picked up by the receiving coil, amplified by the receiving amplifier, detected by the amplitude detector and further amplified, filtered and digitized.
- 25 2. The apparatus according to claim 1, wherein the current passing through the

transmitter coil generates an electromagnetic field in the 6 to 8 kilohertz range with a signal strength on the order of 5 to 8 milliwatts.

3. The apparatus according to claim 1, wherein the metal object to the animal's paw is a small metal annular collar.
4. The apparatus according to claim 1, wherein the metal object to the animal's paw is a small metal "C" collar in incomplete annular form.
- 10 5. The apparatus according to claim 1, wherein the metal object comprises a ferrous metal.
6. The apparatus according to claim 1, wherein the metal object comprises a non-ferrous metal.
- 15 7. The apparatus according to claim 1, wherein the observation chamber is a transparent cylindrical container, insuring that the animal will remain inside the boundaries of the electromagnetic field generated by the coil assembly.
- 20 8. The apparatus according to claim 1, wherein the observation chamber has individual compartments permitting testing of a plurality of animals.
9. The apparatus according to claim 1, wherein the detection assembly below the observation chamber has multiple independent detection units.
- 25 10. The apparatus according to claim 1, wherein the observation chamber is constructed of any rigid transparent plastic.

11. A method for measuring a flinch response by an animal whose paw has been subjected to an irritant, comprising:

attaching a metal object to the animal's paw;

5 placing the animal in an observation chamber situated directly over a detection assembly having

a transmitting oscillator for generating electrical current,

10 an electromagnetic transmitter coil coupled to the oscillator for generating an electromagnetic field;

15 an electromagnetic receiving coil that receives the generated electrical current;

a receiving amplifier that amplifies the received generated electrical current;

an amplitude detector; and

20 15 an amplifier for amplifying the amplitude detected,

wherein the current generated by the transmitting oscillator circulates in the transmitter coil, creating an electromagnetic field that penetrates the metal object attached to the animal's paw, creating fluctuating eddy currents perturbing the electromagnetic field,

25 wherein said fluctuating perturbations are picked up by the receiving coil, amplified by the receiving amplifier, and detected by the amplitude detector, and wherein said perturbations are further amplified, filtered and digitized to produce a measured response to the irritant.

25 12. A method for measuring a flinch response to pain by an animal whose paw has been subjected to an irritant, comprising:

attaching a metal object to the animal's paw;

placing the animal in an observation chamber situated directly over a detection assembly;

generating electrical current by a transmitting oscillator;

generating an electromagnetic field by an electromagnetic transmitter coil

5 coupled to the oscillator;

receiving the generated electromagnetic field by a receiving coil;

amplifying the received generated electrical current by a receiving amplifier having,

an amplitude detector; and

10 an amplifier for amplifying the amplitude detected,

wherein the current generated by the transmitting oscillator circulates in the transmitter coil, creating an electromagnetic field that penetrates the metal object attached to the animal's paw, creating fluctuating eddy currents perturbing the electromagnetic field,

15 wherein said fluctuating perturbations are picked up by the receiving coil, amplified by the receiving amplifier, and detected by the amplitude detector, and wherein said perturbations are further amplified, filtered and digitized to produce a measured response to the irritant.

## REFERENCES

1. Abbadie, C., B. K. Taylor, M. A. Peterson, and A. I. Basbaum: Differential contribution of the two phases of the formalin test to the pattern of c-fos expression in the rat spinal cord: studies with remifentanil and lidocaine. *Pain* 69:101-10, 1997

5

2. Abbott, F. V., K. B. Franklin, and R. F. Westbrook: The formalin test: scoring properties of the first and second phases of the pain response in rats. *Pain* 60:91-102, 1995

10

3. Abram, S. E., and T. L. Yaksh: Morphine, but not inhalation anesthesia, blocks post-injury facilitation. The role of preemptive suppression of afferent transmission. *Anesthesiology* 78:713-21, 1993

15

4. Abram, S. E., and T. L. Yaksh: Systemic lidocaine blocks nerve injury-induced hyperalgesia and nociceptor-driven spinal sensitization in the rat. *Anesthesiology* 80:383-91; discussion 25A, 1994

20

5. Aloisi, A. M., M. E. Albonetti, and G. Carli: Behavioural effects of different intensities of formalin pain in rats. *Physiol Behav* 58:603-10, 1995

6. Bannon, A. W., M. W. Decker, P. Curzon, M. J. Buckley, D. J. Kim, R. J. Radek, J. K. Lynch, J. T. Wasicak, N. H. Lin, W. H. Arnold, M. W. Holladay, M. Williams, and S. P. Arneric: ABT-594 [(R)-5-(2-azetidinylmethoxy)-2-chloropyridine]: a novel, orally effective antinociceptive agent acting via neuronal nicotinic acetylcholine receptors: II. In vivo characterization. *J Pharmacol Exp Ther*

25

285:787-94, 1998

7. Bhatnagar, S., M. F. Dallman, R. E. Roderick, A. I. Basbaum, and B. K. Taylor: The effects of prior chronic stress on cardiovascular responses to acute restraint and formalin injection. *Brain Research* 797:313-20, 1998
- 5
8. Brennan, T. J.: AMPA/kainate receptor antagonists as novel analgesic agents [editorial;comment]. *Anesthesiology* 89:1049-51, 1998
- 10
9. Buerkle, H., M. Marsala, and T. L. Yaksh: Effect of continuous spinal remifentanil infusion on behaviour and spinal glutamate release evoked by subcutaneous formalin in the rat. *British Journal of Anaesthesia* 80:348-53, 1998
- 15
10. Chaplan, S. R., A. B. Malmberg, and T. L. Yaksh: Efficacy of spinal NMDA receptor antagonism in formalin hyperalgesia and nerve injury evoked allodynia in the rat. *Journal of Pharmacology and Experimental Therapeutics* 280:829-38, 1997
- 20
11. Clavelou, P., R. Dallel, T. Orliaguet, A. Woda, and P. Raboisson: The orofacial formalin test in rats: effects of different formalin concentrations. *Pain* 62:295-301, 1995
- 25
- 12.Coderre, T. J., M. E. Fundytus, J. E. McKenna, S. Dalal, and R. Melzack: The formalin test: a validation of the weighted-scores method of behavioural pain rating. *Pain* 54:43-50, 1993
13. Dallel, R., P. Raboisson, P. Clavelou, M. Saade, and A. Woda: Evidence

for a peripheral origin of the tonic nociceptive response to subcutaneous formalin.

*Pain* 61:11-6, 1995

14. Dickenson, A. H., L. C. Stanfa, V. Chapman, and T. L. Yaksh: Response  
5 properties of dorsal horn neurons: Pharmacology of the dorsal horn, in Yaksh, T. L., C. Lynch, III., W. M. Zapol, M. Maze, J. F. Biebuyck, and L. J. Saidman (eds) Anesthesia: Biologic Foundations. Philadelphia: Lippincott-Raven Publishers, 1997, pp 611-624.

10 15. Dickenson, A. H., and A. F. Sullivan: Peripheral origins and central modulation of subcutaneous formalin- induced activity of rat dorsal horn neurones. *Neurosci Lett* 83:207-11, 1987

15 16. Dirig, D. M., and T. L. Yaksh: Intrathecal baclofen and muscimol, but not midazolam, are antinociceptive using the rat-formalin model. *Journal of Pharmacology and Experimental Therapeutics* 275:219-27, 1995

20 17. Dray, A., and A. Dickenson: Systemic capsaicin and olvanil reduce the acute algogenic and the late inflammatory phase following formalin injection into rodent paw. *Pain* 47:79-83, 1991

25 18. Dubuisson, D., and S. G. Dennis: The formalin test: a quantitative study of the analgesic effects of morphine, meperidine, and brain stem stimulation in rats and cats. *Pain* 4:161-74, 1977

19. Handwerker, H. O.: Electrophysiological mechanisms in inflammatory pain. *Agents and Actions. Supplements* 32:91-9, 1991

20. Hunter, J. C., and L. Singh: Role of excitatory amino acid receptors in the mediation of the nociceptive response to formalin in the rat. *Neurosci Lett* 174:217-21, 1994

5 21. Jett, M. F., and S. Michelson: The formalin test in rat: validation of an automated system. *Pain* 64:19-25, 1996

10 22. Jourdan, D., D. Ardid, L. Bardin, M. Bardin, D. Neuzeret, L. Lanphouthacoul, and A. Eschalier: A new automated method of pain scoring in the formalin test in rats. *Pain* 71:265-70, 1997

15 23. Malmberg, A. B., M. F. Rafferty, and T. L. Yaksh: Antinociceptive effect of spinally delivered prostaglandin E receptor antagonists in the formalin test on the rat. *Neurosci Lett* 173:193-6, 1994

20 24. Malmberg, A. B., and T. L. Yaksh: Antinociceptive actions of spinal nonsteroidal anti-inflammatory agents on the formalin test in the rat. *Journal of Pharmacology and Experimental Therapeutics* 263:136-46, 1992

25 25. Malmberg, A. B., and T. L. Yaksh: Pharmacology of the spinal action of ketorolac, morphine, ST-91, U50488H, and L-PIA on the formalin test and an isobolographic analysis of the NSAID interaction [see comments]. *Anesthesiology* 79:270-81, 1993

26. Malmberg, A. B., and T. L. Yaksh: Spinal nitric oxide synthesis inhibition blocks NMDA-induced thermal hyperalgesia and produces antinociception in the formalin test in rats. *Pain* 54:291-300, 1993

27. Malmberg, A. B., and T. L. Yaksh: Effect of continuous intrathecal infusion of omega-conopeptides, N-type calcium-channel blockers, on behavior and antinociception in the formalin and hot-plate tests in rats. *Pain* 60:83-90, 1995

5 28. Nozaki-Taguchi, N., and T. L. Yaksh: A novel model of primary and secondary hyperalgesia after mild thermal injury in the rat. *Neurosci Lett* 254:25-28, 1998

10 29. Peterson, M. A., A. I. Basbaum, C. Abbadie, D. S. Rohde, W. R. McKay, and B. K. Taylor: The differential contribution of capsaicin-sensitive afferents to behavioral and cardiovascular measures of brief and persistent nociception and to Fos expression in the formalin test. *Brain Research* 755:9-16, 1997

15 30. Prado, W. A., and A. S. Goncalves: Antinociceptive effect of intrathecal neostigmine evaluated in rats by two different pain models. *Braz J Med Biol Res* 30:1225-31, 1997

20 31. Price, D. D., G. J. Bennett, and A. Rafii: Psychophysical observations on patients with neuropathic pain relieved by a sympathetic block. *Pain* 36:273-88, 1989

25 32. Puig, S., and L. S. Sorkin: Formalin-evoked activity in identified primary afferent fibers: systemic lidocaine suppresses phase-2 activity. *Pain* 64:345-55, 1996

33. Raboisson, P., R. Dallel, P. Clavelou, B. J. Sessle, and A. Woda: Effects of subcutaneous formalin on the activity of trigeminal brain stem nociceptive

neurones in the rat. *Journal of Neurophysiology* 73:496-505, 1995

34. Shimoyama, N., M. Shimoyama, A. M. Davis, C. E. Inturrisi, and K. J.

Elliott: Spinal gabapentin is antinociceptive in the rat formalin test. *Neurosci Lett*

5 222:65-7, 1997

35. Simmons, R. M., D. L. Li, K. H. Hoo, M. Deverill, P. L. Ornstein, and S.

Iyengar: Kainate GluR5 receptor subtype mediates the nociceptive response to

formalin in the rat. *Neuropharmacology* 37:25-36, 1998

10

36. Singh, L., M. J. Field, P. Ferris, J. C. Hunter, R. J. Oles, R. G. Williams, and

G. N. Woodruff: The antiepileptic agent gabapentin (Neurontin) possesses

anxiolytic- like and antinociceptive actions that are reversed by D-serine.

*Psychopharmacology (Berl)* 127:1-9, 1996

15

37. Tallarida, R. J., and R. B. Murray. Manual of Pharmacologic Calculations

With Computer Programs. (2nd ed.) New York: Springer-Verlag, 1987:291.

38. Taylor, B. K., S. F. Akana, M. A. Peterson, M. F. Dallman, and A. I.

20 Basbaum: Pituitary-adrenocortical responses to persistent noxious stimuli in the awake rat: endogenous corticosterone does not reduce nociception in the formalin test. *Endocrinology* 139:2407-13, 1998

39. Taylor, B. K., M. A. Peterson, and A. I. Basbaum: Persistent cardiovascular

25 and behavioral nociceptive responses to subcutaneous formalin require peripheral nerve input. *Journal of Neuroscience* 15:7575-84, 1995

40. Taylor, B. K., M. A. Peterson, and A. I. Basbaum: Early nociceptive events influence the temporal profile, but not the magnitude, of the tonic response to subcutaneous formalin: effects with remifentanil. *Journal of Pharmacology and Experimental Therapeutics* 280:876-83, 1997

5

41. Tjolsen, A., O. G. Berge, S. Hunskaar, J. H. Rosland, and K. Hole: The formalin test: an evaluation of the method [see comments]. *Pain* 51:5-17, 1992

42. Wheeler-Aceto, H., and A. Cowan: Standardization of the rat paw formalin test for the evaluation of analgesics. *Psychopharmacology* 104:35-44, 1991

10 43. Wheeler-Aceto, H., F. Porreca, and A. Cowan: The rat paw formalin test: comparison of noxious agents. *Pain* 40:229-38, 1990

15 44. Woolf, C. J.: Long term alterations in the excitability of the flexion reflex produced by peripheral tissue injury in the chronic decerebrate rat. *Pain* 18:325-43, 1984

45. Yaksh, T. L.: Preclinical models of nociception, in Yaksh, T. L., C. Lynch, III., W. M. Zapol, M. Maze, J. F. Biebuyck, and L. J. Saidman (eds) *Anesthesia: Biologic Foundations*. Philadelphia: Lippincott-Raven Publishers, 1997, pp 685-718. vol I).

20 25 46. Yaksh, T. L., D. H. Farb, S. E. Leeman, and T. M. Jessell: Intrathecal capsaicin depletes substance P in the rat spinal cord and produces prolonged thermal analgesia. *Science* 206:481-3, 1979

47. Yaksh, T. L., X. Y. Hua, I. Kalcheva, N. Nozaki-Taguchi, and M. Marsala: The spinal biology in humans and animals of pain states generated by persistent small afferent input. *Proceedings of the National Academy of Sciences of the United States of America* 96:7680-6, 1999

5

48. Yaksh, T. L., and A. B. Malmberg: Central pharmacology of nociceptive transmission, in Wall, P., and M. R. (eds) *Textbook of Pain*. 4th ed. Edinburgh, UK: Churchill Livingstone, 1999, pp 253-308.

10 49. Yaksh, T. L., and T. A. Rudy: Chronic catheterization of the spinal subarachnoid space. *Physiol Behav* 17:1031-1036, 1976

15 50. Yamamoto, T., and T. L. Yaksh: Stereospecific effects of a nonpeptidic NK1 selective antagonist, CP-96,345: antinociception in the absence of motor dysfunction. *Life Sci* 49:1955-63, 1991

51. Yoon, M. H., and T. L. Yaksh: The effect of intrathecal gabapentin on pain behavior and hemodynamics on the formalin test in the rat. *Anesthesia and Analgesia* 89:434-9, 1999

20

52. Zar, J. H. *Biostatistical Analysis*. (2nd ed.) Englewood Cliffs, NJ: Prentice-Hall, Inc., 1984

25